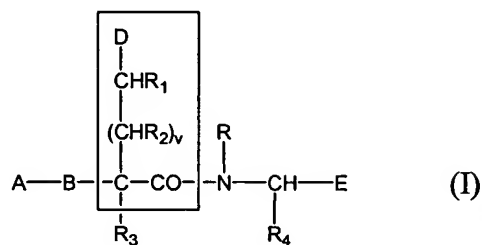


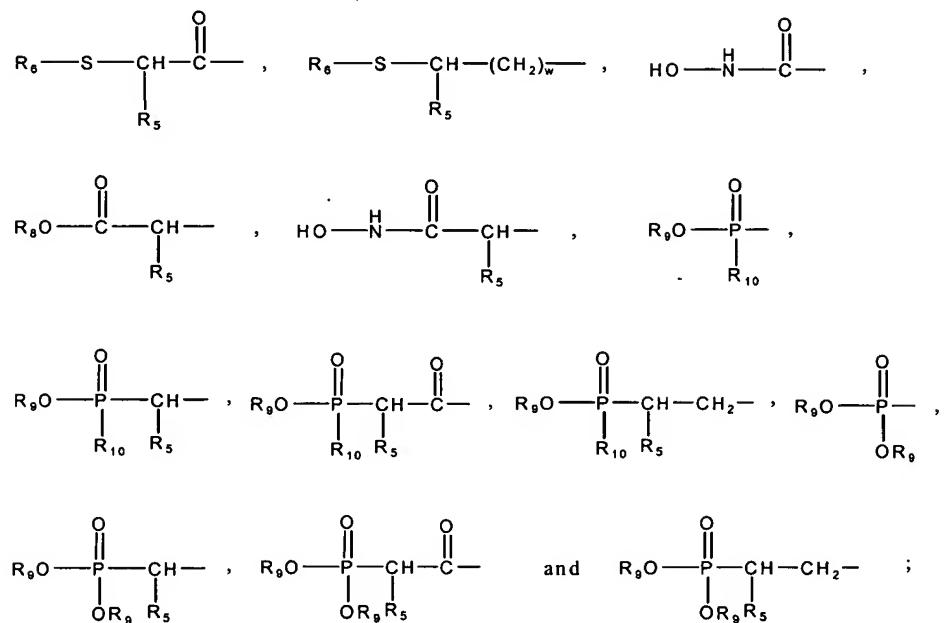
# WHAT IS CLAIMED:

1. A compound comprising Formula (I), or a pharmaceutically acceptable salt thereof:



wherein

A is a zinc ligand or zinc ligand bearing moiety selected from the group consisting of:



B is  $\begin{array}{c} \text{R}_{11} \\ | \\ \text{---N---} \end{array}$  ,  $\text{---CH}_2\text{---}$  or absent ;

R is hydrogen or lower alkyl;

R<sub>1</sub> is hydrogen or lower alkyl;

R<sub>2</sub> is hydrogen, or lower alkyl;

R<sub>3</sub> is hydrogen or lower alkyl;

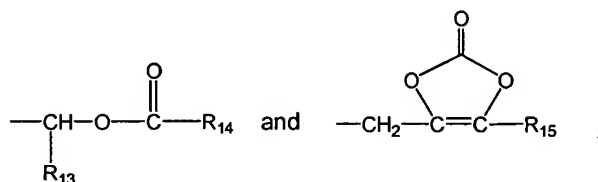
R<sub>4</sub> is lower alkyl, substituted lower alkyl, cycloalkyl-(CH<sub>2</sub>)<sub>w</sub>-, aryl-(CH<sub>2</sub>)<sub>w</sub>-, substituted aryl -(CH<sub>2</sub>)<sub>w</sub>- or heteroaryl-(CH<sub>2</sub>)<sub>w</sub>-;

R<sub>5</sub> is hydrogen, lower alkyl, substituted lower alkyl, cycloalkyl-(CH<sub>2</sub>)<sub>x</sub>-, aryl-(CH<sub>2</sub>)<sub>x</sub>-, substituted aryl-(CH<sub>2</sub>)<sub>x</sub>-, or heteroaryl-(CH<sub>2</sub>)<sub>x</sub>-;

R<sub>6</sub> is hydrogen, R<sub>7</sub>-CO-, or R<sub>12</sub>-S-;

R<sub>7</sub> is alkyl, substituted alkyl, cycloalkyl-(CH<sub>2</sub>)<sub>y</sub>-, aryl-(CH<sub>2</sub>)<sub>y</sub>-, substituted aryl-(CH<sub>2</sub>)<sub>y</sub>- or heteroaryl-(CH<sub>2</sub>)<sub>y</sub>-;

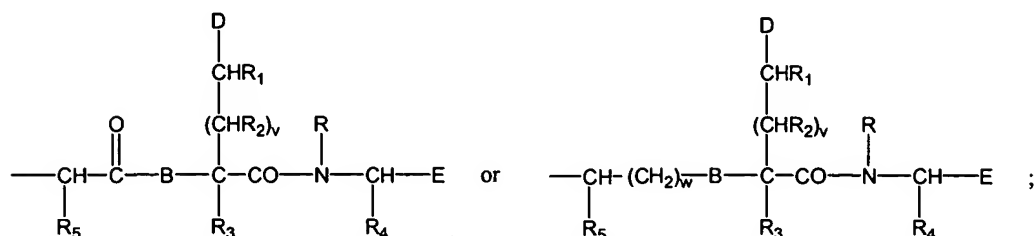
R<sub>8</sub> and R<sub>9</sub> are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl-(CH<sub>2</sub>)<sub>y</sub>-, substituted aryl-(CH<sub>2</sub>)<sub>y</sub>-, heteroaryl-(CH<sub>2</sub>)<sub>y</sub>-;



R<sub>10</sub> is alkyl, substituted alkyl, cycloalkyl-(CH<sub>2</sub>)<sub>y</sub>-, aryl-(CH<sub>2</sub>)<sub>y</sub>-, substituted aryl-(CH<sub>2</sub>)<sub>y</sub>- or heteroaryl-(CH<sub>2</sub>)<sub>y</sub>-;

R<sub>11</sub> is hydrogen or lower alkyl;

R<sub>12</sub> is alkyl, substituted alkyl, cycloalkyl-(CH<sub>2</sub>)<sub>y</sub>-, aryl-(CH<sub>2</sub>)<sub>y</sub>-, substituted aryl-(CH<sub>2</sub>)<sub>y</sub>-, heteroaryl-(CH<sub>2</sub>)<sub>y</sub>-,



in which case -S-R<sub>12</sub> completes a symmetrical disulfide;

R<sub>13</sub> is hydrogen, lower alkyl, cycloalkyl or phenyl;

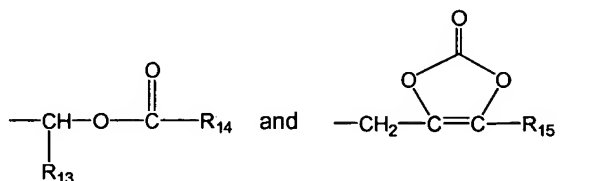
R<sub>14</sub> is hydrogen, lower alkyl, lower alkoxy or phenyl;

R<sub>15</sub> is lower alkyl or aryl-(CH<sub>2</sub>)<sub>y</sub>-;

D is -COOH, -SO<sub>2</sub>H, -SO<sub>3</sub>H, -PO<sub>3</sub>H<sub>2</sub>, -OSO<sub>3</sub>H or -OPO<sub>3</sub>H<sub>2</sub>;

E is hydrogen, R<sub>12</sub>, -COOH, -CONH<sub>2</sub>, -CONH(lower alkyl), -CON(lower alkyl)<sub>2</sub>, -CONH-(CH<sub>2</sub>)<sub>z</sub>-aryl, -CON(-(CH<sub>2</sub>)<sub>z</sub>-aryl)<sub>2</sub>, -CO-amino acid, -CH<sub>2</sub>COOH, CH<sub>2</sub>OH, -CH<sub>2</sub>CH<sub>2</sub>OH, or -COOR<sub>16</sub>;

R<sub>16</sub> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl-(CH<sub>2</sub>)<sub>y</sub>-, substituted aryl-(CH<sub>2</sub>)<sub>y</sub>-, heteroaryl-(CH<sub>2</sub>)<sub>y</sub>-,



C is carbon;

H is hydrogen;

O is oxygen;

N is nitrogen;

S is sulfur;

P is phosphorus;

v is zero or one;

w is zero or an integer ranging from 1 to 4;

x is an integer ranging from 1 to 4;

y is zero or an integer ranging from 1 to 6; and

z is zero, one, two, or three.

2. The compound of claim 1, wherein  $R_1$ , when  $v=1$ , is connected to the carbon bearing  $R_2$  to form an alkylene bridge of 1 carbon atom, representing with the carbon atom to which it is attached a cyclopropane ring.
3. The compound of claim 1, wherein  $R_2$ , when  $v=1$ , is connected to the carbon bearing  $R_1$  to form an alkylene bridge of 1 carbon atom representing with the carbon atom to which it is attached a cyclopropane ring.
4. The compound of claim 1, wherein  $R_1$ , when  $v=1$ , is connected to the carbon bearing  $R_3$  to form an alkylene bridge of 1 carbon atom, representing with the carbon atom to which it is attached a cyclobutane ring.
5. The compound of claim 1, wherein  $R_3$ , when  $v=1$ , is connected to the carbon bearing  $R_1$  to form an alkylene bridge of 1 carbon atom, representing with the carbon atom to which it is attached a cyclobutane ring.
6. The compound of claim 1, wherein  $R_1$  and  $R_3$ , when  $v=1$ , are connected together to form an alkylene bridge of 2 carbon atoms representing with the carbon atoms to which they are attached a cyclopentane ring.
7. The compound of claim 1, wherein  $R_1$  and  $R_3$ , when  $v=0$ , are connected together to form an alkylene bridge of 3 carbon atoms representing with the carbon atoms to which they are attached a cyclopentane ring.

8. The compound of claim 1, wherein  $R_1$  and  $R_3$ , when  $v=0$ , are connected together to form an alkylene bridge of 4 carbon atoms representing with the carbon atoms to which they are attached a cyclohexane ring.
9. The compound of claim 1, wherein  $R_1$  and  $R_3$ , when  $v=1$ , are connected together to form an alkylene bridge of 3 carbon atoms representing with the carbon atoms to which they are attached a cyclohexane ring.
10. The compound of claim 1, wherein  $R$  and  $R_4$  are connected together to form an alkylene bridge of 3 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a pyrrolidine ring.
11. The compound of claim 1, wherein  $R$  and  $R_4$  are connected together to form an alkylene bridge of 4 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a piperidine ring.
12. The compound of claim 1, wherein  $R_1$  and  $R_{11}$ , when  $v=0$ , are connected together to form an alkylene bridge of 3 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a piperidine ring.
13. The compound of claim 1, wherein  $R_1$  and  $R_{11}$ , when  $v=1$ , are connected together to form an alkylene bridge of 2 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a piperidine ring.
14. The compound of claim 1, wherein  $R_2$  and  $R_{11}$ , when  $v=1$ , are connected together to form an alkylene bridge of 2 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a pyrrolidine ring; the alkylene bridge may be substituted by a lower alkyl or alkenyl group at either carbon.

15. The compound of claim 1, wherein  $R_{11}$  is hydrogen or lower alkyl and wherein the carbon bearing  $R_1$  and the nitrogen bearing  $R_{11}$ , when  $v=1$ , are directly connected together to form an azetidine ring.
  
16. The compound of claim 1, wherein the compound is further defined as N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-acetyl-amino)-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-3-phenyl-propionyl amino)-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-propionyl-amino)-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-4-methyl-pentanoyl-amino)-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-3-methyl-butyryl-amino)-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(3-hydroxy-2-mercapto-propionyl-amino)-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(3-hydroxy-2-mercapto-butyryl-amino)-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-hexanoyl-amino)-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-4-phenyl-butyryl-amino)-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-2-phenyl-acetyl-amino)-succinamic acid, 3-(3-Biphenyl-4-yl-2-mercapto-propionyl-amino)-N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-succinamic acid, 3-(3-(4-Benzyloxy-phenyl)-2-mercapto-propionyl-amino)-N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-[3-(4-fluoro-phenyl)-2-mercapto-propionyl-amino]-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-[2-mercapto-3-(4-methoxy-phenyl)-propionyl-amino]-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(3-cyclohexyl-2-mercapto-propionyl-amino)-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-[3-(1H-indol-3-yl)-2-mercapto-propionyl-amino]-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-3-naphthalen-2-yl-propionyl-amino)-succinamic acid, N-(1-Carboxy-2-naphthalen-2-yl-ethyl)-3-(2-mercapto-3-phenyl propionyl-amino)-succinamic acid, N-(1-Carboxy-2-hydroxy-ethyl)-3-(2-mercapto-3-phenyl-propionyl amino)-succinamic acid, N-[1-Carboxy-2-(4-hydroxy-phenyl)-ethyl]-3-(2-mercapto-3-phenyl-propionyl-amino)-succinamic acid, N-[1-Carboxy-2-phenyl-

ethyl)-3-(2-mercapto-3-phenyl-propionyl amino)-succinamic acid, N-(2-Biphenyl-4-yl-1-Carboxy-ethyl)-3-(2-mercapto-3-phenyl-propionyl amino)-succinamic acid, N-(1-Benzyl-2-hydroxy-ethyl)-3-(2-mercapto-3-phenyl-propionyl amino)-succinamic acid, N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-3-phenyl-propionylamino)-succinamic acid, 4-[1-Carboxy-2-(1H-indol-3-yl)-ethylcarbamoyl]-4-(2-mercapto-3-phenyl-propionylamino)-ethyl]-butyric acid, N-[2-(1H-indol-3-yl)-methylcarbamoyl-ethyl]-3-(2-mercapto-acetyl amino)-succinamic acid, N-[1-(1-Carboxy-2-hydroxy-ethylcarbamoyl)-2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-3-phenyl-propionylamino)-succinamic acid, N-[2-(1H-indol-3-yl)-methoxycarbonyl-ethyl]-3-(2-mercapto-acetyl amino)-succinamic acid, N-[2-(1H-indol-3-yl)-ethyl]-3-(2-mercapto-3-phenyl-propionylamino)-succinamic acid, 3-(2-Biphenyl-4-yl-ethylcarbamoyl)-4-hydroxycarbamoyl-butyric acid, 3-[2-(4'-Cyano-biphenyl-4-yl)-ethylcarbamoyl]-4-hydroxycarbamoyl-butyric acid, 4-Hydroxycarbamoyl-3-[2-(4-pyridin-2-yl-phenyl)-ethylcarbamoyl]-butyric acid, 4-Hydroxycarbamoyl-3-(4-phenyl-butylcarbamoyl)-butyric acid, 4-Hydroxycarbamoyl-3-(2-phenoxy-ethylcarbamoyl)-butyric acid, 3-[2-(4'-Hydroxy-biphenyl-4-yl)-ethylcarbamoyl]-4-hydroxycarbamoyl-butyric acid, 3-(2,2-Diphenyl-ethylcarbamoyl)-4-hydroxycarbamoyl-butyric acid, 3-[2-(4'-Dimethylamino-biphenyl-4-yl)-ethylcarbamoyl]-4-hydroxycarbamoyl-butyric acid, 4-Hydroxycarbamoyl-3-(5-hydroxy-pentylcarbamoyl)-butyric acid, 3-[(Biphenyl-4-ylmethyl)-carbamoyl]-4-hydroxycarbamoyl-butyric acid, 3-(2-Biphenyl-4-yl-ethylcarbamoyl)-5-hydroxycarbamoyl-pentanoic acid, N-[1-carboxy-2-(1H-indol-3-yl)-ethyl]-3-(3-phenyl-1-phosphono-propylamino)-succinic acid, or 3-(2-Naphthalen-2-yl-ethylcarbamoyl)-pentanedioic acid.

17. The compound of claim 16, wherein the compound is further defined as 3-(2-Biphenyl-4-yl-ethylcarbamoyl)-4-hydroxycarbamoyl-butyric acid.
18. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 and a physiologically acceptable carrier or excipient.

19. The pharmaceutical composition of claim 18, wherein the compound of claim 1 is further defined as a compound of claim 16.
20. The pharmaceutical composition of claim 18, wherein the compound of claim 1 is further defined as the compound of claim 17.
21. A method for inhibiting PHEX comprising contacting PHEX with an inhibitory amount of a compound of claim 1.
22. The method of claim 21, wherein the compound of claim 1 is further defined as the compound of claim 16.
23. The method of claim 21, wherein the compound of claim 1, is further defined as the compound of claim 17.
24. A method for stimulating bone mass formation in a mammal comprising inhibiting PHEX with an effective amount of a compound of 1.
25. The method of claim 24, wherein the compound of claim 1 is further defined as the compound of claim 16.
26. The method of claim 24, wherein the compound of claim 1 is further defined as the compound of claim 17.
27. A method for treating or preventing a disease or condition associated with a phosphate metabolism defect comprising administering an effective amount of a compound of claim 1 to a mammal in need thereof.



28. The method of claim 27, wherein said disease or condition is selected from the group consisting of hyperphosphatemia, hyperparathyroidism, and renal insufficiencies.
29. The method of claim 27, wherein the compound of claim 1 is further defined as the compound of claim 16.
30. The method of claim 27, wherein the compound of claim 1 is further defined as the compound of claim 17.
31. A method for identifying a PHEX substrate comprising:
- (a) contacting a candidate with PHEX in the presence and in the absence of a compound of claim 1; and
  - (b) assessing PHEX biological activity of the candidate in the presence and absence of the compound,
- wherein the candidate compound is selected as a PHEX substrate when PHEX biological activity is measurably higher in the absence versus in the presence of the compound.
32. The method of claim 31, wherein the compound of claim 1 is further defined as the compound of claim 16.
33. The method of claim 31, wherein the compound of claim 1 is further defined as the compound of claim 17.